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(54) Title: SINGLE NUCLEOTIDE POLYMORPHISMS IN GENES

(57) Abstract: The invention provides nucleic acid segments of the human genome, particularly nucleic acid segments from a gene, including polymorphic sites. Allele-specific primers and probes hybridizing to regions flanking or containing these sites are also provided. The nucleic acids, primers and probes are used in applications such as phenotype correlations, forensics, paternity testing, medicine and genetic analysis. A role for the thrombospondin gene(s) in vascular disease is also disclosed. Use of single nucleotide polymorphisms in the thrombospondin gene(s) for diagnosis, prediction of clinical course and treatment response, development of therapeutics and development of cell-culture-based and animal models for research and treatment are disclosed.

INTERNATIONAL SEARCH REPORT

 Int: Application No
 PCT/US 00/24503

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C12Q1/68 C07K14/47 C07K14/78

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C07K C12Q

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

MEDLINE, SEQUENCE SEARCH, BIOSIS, EPO-Internal

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 5 750 502 A (KLAR AVIHU ET AL) 12 May 1998 (1998-05-12) SEQ ID NO:20	1-30
A	POLYMEROPOULOS M H ET AL: "DINUCLÉOTIDE REPEAT POLYMORPHISM AT THE HUMAN THROMBOSPONDIN GENE THBS1" NUCLEIC ACIDS RESEARCH, vol. 18, no. 24, 1990, page 7467 XP002188932 ISSN: 0305-1048 abstract --- -/--	1-30

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

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INTERNATIONAL SEARCH REPORT

Inter ☐ if Application No
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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WANG D G ET AL: "Large-scale identification, mapping, and genotyping of single-nucleotide polymorphisms in the human genome" SCIENCE, AMERICAN ASSOCIATION FOR THE ADVANCEMENT OF SCIENCE,, US, vol. 280, 1998, pages 1077-1082, XP002089398 ISSN: 0036-8075 the whole document ---	1-30
A	FAN J ET AL: "Genetic mapping: Finding and analyzing single-nucleotide polymorphisms with high-density DNA arrays" AMERICAN JOURNAL OF HUMAN GENETICS, UNIVERSITY OF CHICAGO PRESS, CHICAGO,, US, vol. 61, no. 4, SUPPL, 1 October 1997 (1997-10-01), page 1601 XP002089397 ISSN: 0002-9297 abstract -----	1-30

INTERNATIONAL SEARCH REPORT

international application No.
PCT/US 00/24503

Box I Observations where certain claims were found unsearchable (Continuation of Item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☐ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of Item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

1-30

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

Invention 1, claims 1-30

A method for predicting or diagnosing a vascular disease comprising; determining the nucleotide present at position 2210 of the thrombospondin 1 gene (SEQ ID NO:1). A nucleic acid molecule, a peptide (SEQ ID NO:2). A method for predicting or diagnosing a vascular disease comprising; determining the amino acid at position 700 of thrombospondin-1.

Invention 2, claims 31-60

A method for predicting or diagnosing a vascular disease comprising; determining the nucleotide present at position 2210 of the thrombospondin-4 gene (SEQ ID NO:3). A nucleic acid molecule, a peptide (SEQ ID NO:4). A method for predicting or diagnosing a vascular disease comprising; determining the amino acid at position 700 of thrombospondin-4.

Inventions 3 - 2547, claims 61-72

A nucleic acid molecule, an isolated gene product. A method of analyzing a nucleic acid sample. Every invention is characterised by each individual sequence of table 1 (corresponding to SEQ ID NO: 7-2551).

INTERNATIONAL SEARCH REPORT

Inte I Application No
PCT/US 00/24503

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
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